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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/418,870 04/07/95 VAN NEST

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EXAMINER

WORTMAN, D

ART UNIT

PAPER NUMBER

1648

DATE MAILED:

08/30/00

65

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
08/418,870

Applicant(s)
Van Nest et al.

Examiner
Donna C. Wortman, Ph.D.

Group Art Unit
1648



☒ Responsive to communication(s) filed on 6/14/00 and 6/27/00

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-5, 7-9, 29, 36, and 38-51 is/are pending in the application

Of the above, claim(s) _____ is/are withdrawn from consideration

☒ Claim(s) 29 and 40-50 is/are allowed.

☒ Claim(s) 1-5, 7-9, 36, 38, 39, and 51 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 64

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

Art Unit: 1648

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1648.

Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's second submission after final filed on 6/14/00 has been entered.

The amendment and documents submitted 6/14/00 were not entered according to Applicant's request. The preliminary amendment and the accompanying documents submitted 6/26/00 have been entered; in that preliminary amendment, Claims 1 and 29 were amended and new claims 40-51 were added. Consequently, claims 1-5, 7-9, 29, 36, and 38-51 are pending and under examination at this time.

All documents listed by Applicant on the PTO 1449 submitted on 6/27/00 have been considered by the Examiner as indicated by the Examiner's initials. Certain of the documents have been lined through and will not appear on the face of any patent that issues on this application since they are not publications.

Substitute declarations submitted 6/27/00 have been received and made of record.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought

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to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-5, 7-9, 36, 38, 39, and 51 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Woodard et al. in view of Silvestri et al., for reasons of record in rejecting claims 1-5, 7-9, 36, 38, and 39 in the previous Office action. Woodard discloses an adjuvant composition comprising a metabolizable oil (hexadecane, as exemplified, or, alternatively, soybean or peanut oil, squalene, and squalane are also disclosed as metabolizable oils) and an emulsifying agent (a polyoxyethylene sorbitan mono-, di- or trioleate or a sorbitan mono-, di-, or triester) as an oil-in-water emulsion. These compositions exist in the absence of a polyoxypropylene-polyoxyethylene block copolymer and in the absence of any muramyl peptide. While Woodard does not specifically disclose that "substantially all" of the droplets are less than 1 micron in diameter, insofar as can be ascertained from the copy of Fig. 1 provided, Woodard's droplets appear to be much smaller than the 2.5 μ m calibration line in Fig. 1(a); further, Woodard discloses that small droplet size is a desirable feature of a stable emulsion and so one would have been motivated to use an emulsion with droplet size as small as possible in order to obtain a stable composition. Woodard's composition differs from the claimed composition in that Woodard discloses that a emulsifying agent concentration of less than 4% is likely to result in "creaming" but points out that such creaming is primarily a cosmetic problem and does not interfere with the adjuvant capability of the composition.

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Silvestri et al. disclose the desirability of small, in particular, submicron size droplets for achieving improved stability in oil-in-water emulsions, discloses use of emulsifier concentrations of 0.5-3.0% and disclose a device and method for achieving such submicron droplets even at low surfactant concentrations (see page 142, first paragraph of column 1, and Table 1, for example). Thus it would have been obvious to one of ordinary skill in the art at the time the invention was made to have made and used an adjuvant composition comprising a metabolizable oil and an emulsifying agent wherein said oil and said emulsifying agent are present in the form of an oil-in-water emulsion having oil droplets substantially all of which are 100nm-500nm in diameter, and the concentration of emulsifying agent is 0.01-2.5% w/w, and wherein the composition exists in the absence of block copolymer and muramyl peptide, because of Woodard's disclosure of such adjuvant compositions, together with the disclosure that stable compositions are rather more desirable at least for cosmetic reason, and because Silvestri teaches the means to obtain and the desirability of obtaining smaller droplet size in the presence of emulsifier concentrations that are lower than in the stable emulsions of Woodard.

Applicant has argued that Woodard teaches that a concentration of emulsifier of 4% or greater is required in order to prevent creaming of the emulsion; that Woodard teaches that antigen must be added to the internal phase for optimal antibody response; that Woodard's "preferred" composition does not exist without added antigen; and that Silvestri does not teach that substantially all of the oil droplets are in the claimed size range.

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These arguments have been considered but not found persuasive. While Woodard discloses adding higher emulsifier concentrations than those claimed, Silvestri teaches that a stable emulsion is obtained with emulsifier concentrations well within the claimed range when microfluidization is used to form the emulsion; further, in the absence of evidence to the contrary, it reasonably appears that microfluidization as taught by Silvestri results in the formation of oil droplets of the claimed size range. Both the composition of Woodard and the composition of Silvestri are disclosed to exist without added antigen, even if, in the case of Woodard, it is not the "preferred" form. A reference is available for everything taught therein. The rejected claims are drawn to compositions, and not to methods of raising antibodies.

Claims 29 and 40-50 are allowed. Claims 29 and 40-50 are understood to be drawn to a method of stimulating an immune response in a host animal using an adjuvant-antigen composition in which the antigen is in the external phase of an oil-in-water emulsion which has the claimed properties.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Wortman whose telephone number is (703) 308-1032. The examiner can normally be reached on Monday through Thursday from 8:00 am to 5:30 pm. The examiner can also be reached on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached at (703) 308-4027. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Donna Wortman, Art Unit 1648, and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without

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entry. The Art Unit 1648 FAX telephone number for official papers is (703) 308-4242. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday, or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.



Donna C. Wortman, Ph.D.
Primary Examiner

August 25, 2000